

AD-A248 438



MENTATION PAGE

Form Approved

OMB No. 0704-0188

is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and reviewing the collection of information, sending comments regarding this burden estimate or any other aspect of this collection of information, including this burden estimate, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Avenue, Washington, DC 20540-6001, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

REPORT DATE

1/23/92

3. REPORT TYPE AND DATES COVERED

4. TITLE AND SUBTITLE

Chemical Reactivity and Selectivity in Organized Media

5. FUNDING NUMBERS

6. AUTHOR(S)

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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Laramie, WY 820718. PERFORMING ORGANIZATION
REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U. S. Army Research Office
P. O. Box 12211
Research Triangle Park, NC 27709-221110. SPONSORING/MONITORING
AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

The view, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other documentation.

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

The overall project focused on chemical reactivity and selectivity in organized media. Five parts were completed and published, and two are still underway. The first part of the project involved a study of the use of reversed-phase high performance liquid chromatography (HPLC) columns as chemical reactors, and the second, an investigation of the selectivity of monohalogenation of alkyl phenyl ethers in micellar and vesicular media. The third part comprised a study of the synthesis and characterization of second generation, single-chain, cleavable surfactants. The fourth part involved a study of Diels-Alder reactions of a surfactant 1,3-diene, and the fifth, an investigation of the vesicular and monolayer properties of diastereomeric surfactants. The sixth part involves a study of anionic analogues of the cleavable surfactants of the third part, and the seventh, another study of Diels-Alder reactions of a surfactant 1,3-diene.

14. SUBJECT TERMS

surfactant based organized media; micelles; vesicles
surfactants, cleavable
high performance liquid chromatography

15. NUMBER OF PAGES

8

16. PRICE CODE

17. SECURITY CLASSIFICATION
OF REPORT

UNCLASSIFIED

18. SECURITY CLASSIFICATION
OF THIS PAGE

UNCLASSIFIED

19. SECURITY CLASSIFICATION
OF ABSTRACT

UNCLASSIFIED

20. LIMITATION OF ABSTRACT

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Chemical Reactivity and Selectivity in Organized Media

Final Report

by

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January 23, 1992

U.S. Army Research Office

Contract No. DAAL03-88-K-0030

Department of Chemistry

University of Wyoming

Laramie, WY 82071

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I. Statement of the Problem Studied

The overall project focused on chemical reactivity and selectivity in organized media. Five parts were completed and published, and two are still underway. The first part of the project involved a study of the use of reversed-phase high performance liquid chromatography (HPLC) columns as chemical reactors, and the second, an investigation of the selectivity of monohalogenation of alkyl phenyl ethers in micellar and vesicular media. The third part comprised a study of the synthesis and characterization of second generation, single-chain, cleavable surfactants. The fourth part involved a study of Diels-Alder reactions of a surfactant 1,3-diene, and the fifth, an investigation of the vesicular and monolayer properties of diastereomeric surfactants. The sixth part involves a study of anionic analogues of the cleavable surfactants of the third part, and the seventh, another study of Diels-Alder reactions of a surfactant 1,3-diene.

II. Statement of the Most Important Results

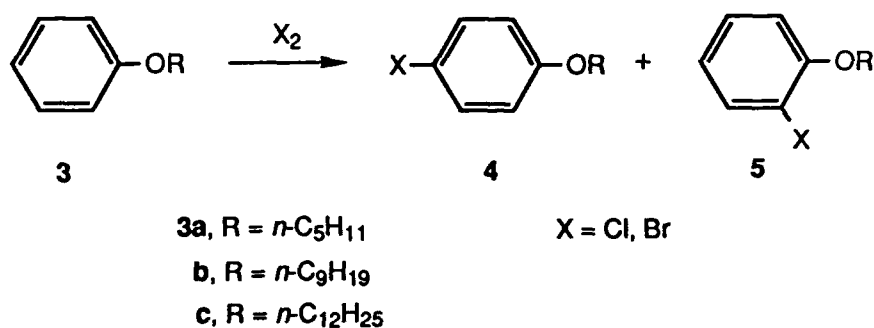
In the first part of the project, the OH^- -catalyzed hydrolyses of *p*-nitrophenyl acetate (1) and hexanoate (2) were performed with excess OH^- on a reversed-phase liquid chromatography column of macroporous 10- μm poly(styrene-divinylbenzene) under HPLC conditions in real time to give pseudo-first-order rate constants k_{Ψ} .¹ The maximum value of k_{Ψ}^1/k_{Ψ}^2 was ≥ 25 , and the reactivity difference was attributed to different rates of desorption of 1 and 2 from the polymer surface into the mobile phase, where OH^- was localized.

The reductions of propiophenone and octanophenone to 1-phenyl-1-propanol and 1-phenyl-1-octanol, respectively, with sodium borohydride and tetrabutylammonium borohydride were performed on the same reversed-phase column as above under HPLC conditions in real time.² In these reactions a lower concentration of the latter reducing agent than of the former was needed to effect the same extent of reduction, and modest substrate selectivity was obtained.

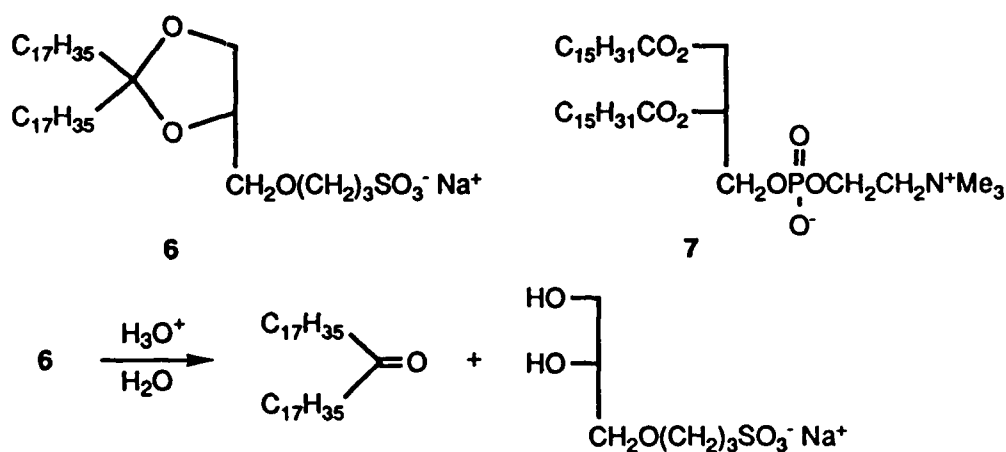
Overall, the results of the first part of the project demonstrated that a polymer-based, reversed-phase HPLC column can impart selectivity to the reactions of an ionic, water-soluble

reagent with neutral, organic substrates that have comparable intrinsic reactivities but different hydrophilic/lipophilic characters.

In the second part of the project, the rates and regioselectivities of monohalogenation of alkyl phenyl ethers **3** by chlorine water and bromine water to give **4** and **5** were determined in micellar sodium dodecyl sulfate and vesicular **6** and **7** in a pH 7.30 phosphate buffer.³ The 4/5 ratios were greater in the surfactant media than in buffer alone and increased in the order **3a** <

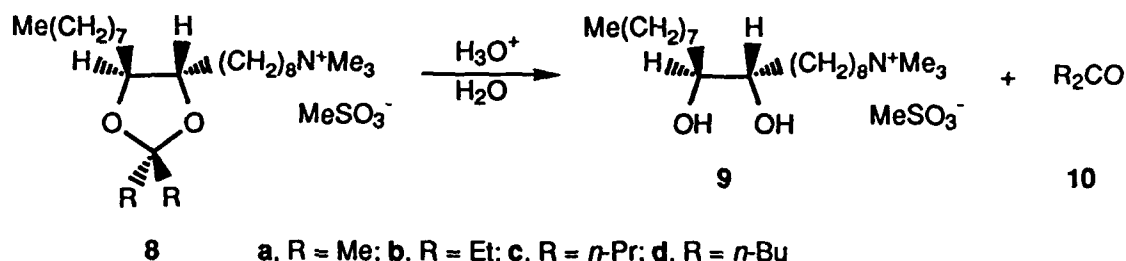


3b < **3c**. In general, the second-order rate constants were less in the surfactant media than in buffer alone and decreased in the order **3a** > **3b** ≥ **3c**. The combination of kinetic and regioselectivity data indicated that the three ethers, which differ in hydrophilic/lipophilic character, have different solubilization sites in the surfactant aggregates and react at these sites. The quantitative isolation of products and unreacted starting material from vesicular **6**, a cleavable surfactant, involved acid-catalyzed hydrolysis of **6**, followed by straightforward extractive workup.

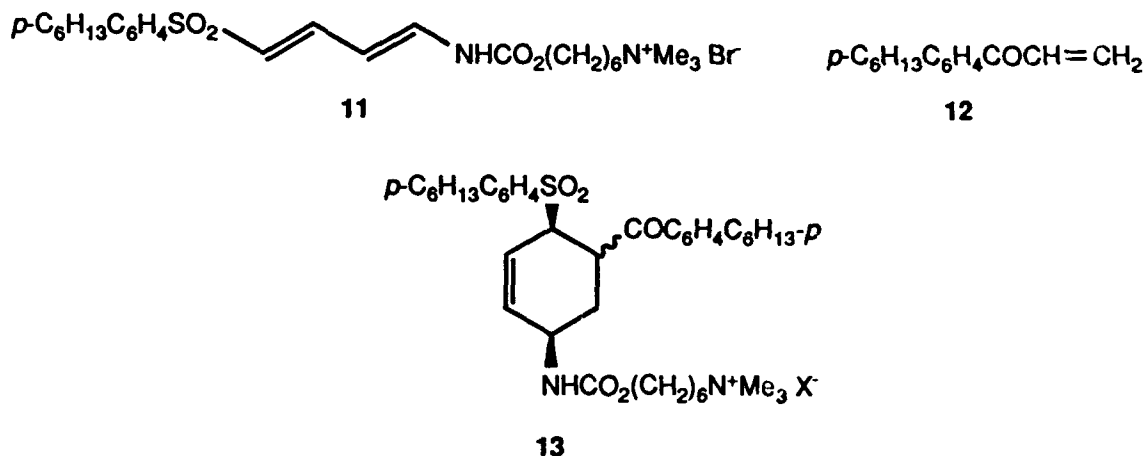


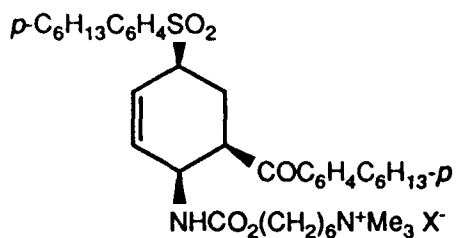
In all of the single, and in most of the double-chain, cleavable surfactants reported previously, the labile linkage separates the major lipophilic and hydrophilic portions. Cleavage

at the linkage results in the formation of two nonsurfactant fragments: a neutral, water-insoluble compound and an ionic, water-soluble compound. In some applications the presence of a *water-insoluble* fragment might present problems. And in others, conversion of the cleavable surfactant into *another surfactant* with different properties could be beneficial. Thus in the third part of the project, we prepared **8** as the first single-chain examples of what we term *second generation* cleavable surfactants.⁴ Such a surfactant can be converted into *another surfactant*, with a *higher critical micelle concentration* (cmc), and a neutral, *water-soluble* compound. Ketal-based surfactants **8** give surfactant **9** and ketones **10** on acid-catalyzed hydrolysis.

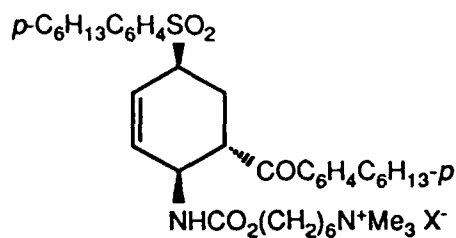


In the third part of the project, the ability of aqueous micelles and reversed micelles to control the regiochemistry of Diels-Alder reactions of **11** and **12** was evaluated.⁵ If **11** and **12** were to react within the micelles in their preferred orientations, cycloadduct **13** would result, as opposed to **14b** and its *exo* isomer **14b**, the theoretically-predicted products actually obtained. The orientational effects in the aggregates were not strong enough to overcome the reaction's intrinsically preferred regiochemistry.



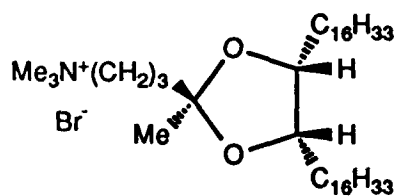


14a

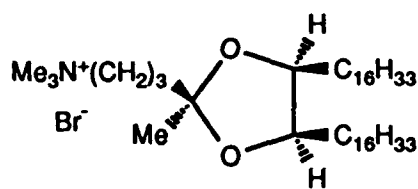


14b

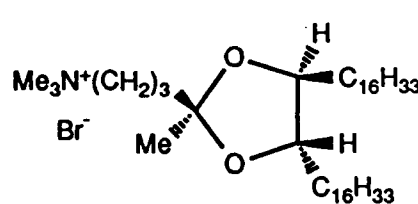
In the fifth part of the project, a study of diastereomeric surfactants centered around the following question: How, if at all, is their diastereomeric nature expressed in vesicular and monolayer form? If the full potential of vesicles as membrane models and storage and release agents is to be realized, it is important to delineate the influence on their properties of such subtle features as the stereochemistry of their constituent surfactants. Three diastereomeric, quaternary ammonium surfactants, **15a**, **15b**, and **15c**, were prepared and the properties of their vesicles and monolayers compared.⁶ The vesicles were characterized by dynamic laser light scattering, differential scanning calorimetry, and [¹⁴C]sucrose entrapment and release studies. Clear differences among the three systems were found in the latter two studies. The phase transition temperature order for both sonicated and vortexed vesicles was **15a** > **15c** > **15b**, and for sonicated vesicles the permeability order was **15b** > **15c** > **15a**. The three surfactants also displayed different monolayer characteristics. The degrees of expansion in the surface pressure-area isotherms, the monolayer stability limits, and the propensities of the films to spread from their crystals followed the same order: **15b** > **15c** > **15a**. Overall, the results suggested that in both vesicular and monolayer form **15a** has the tightest, and **15b** the loosest surfactant packing.



15a



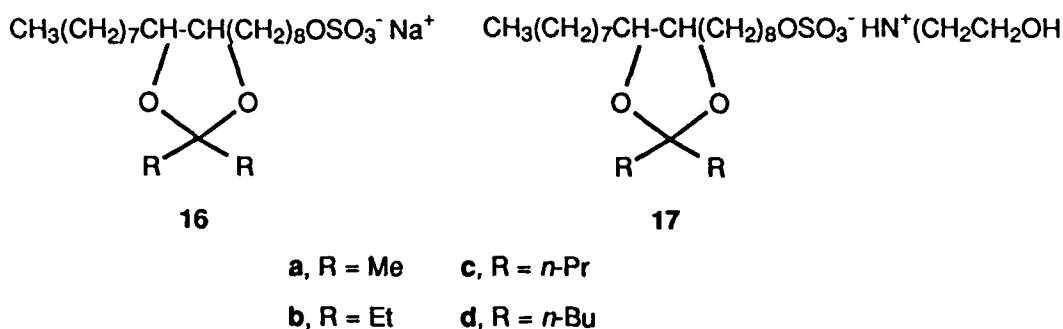
15b



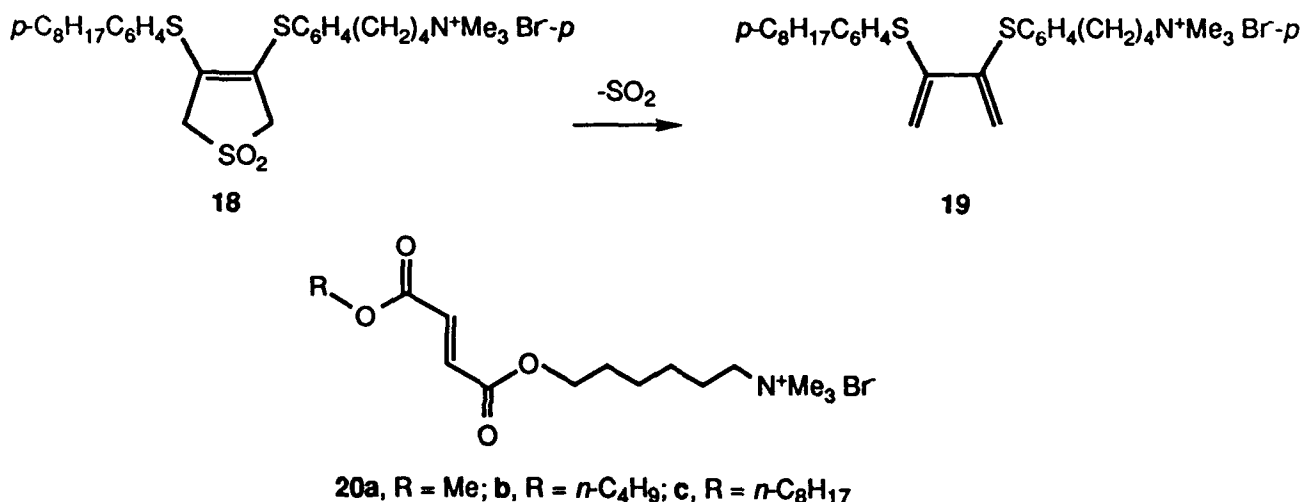
15c

In the sixth part of the project, which is ongoing, we are preparing second generation cleavable surfactant series **16** and **17**.⁷ These anionic surfactants should be much more

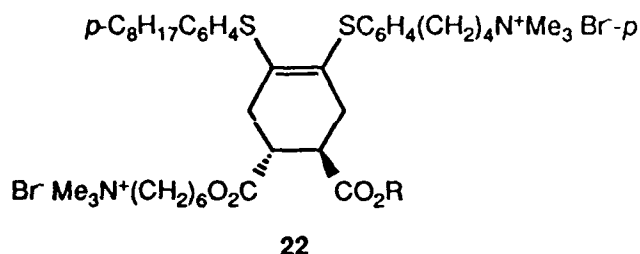
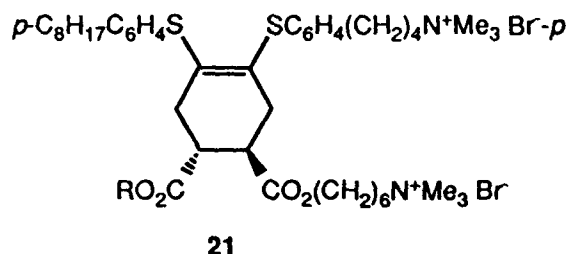
for practical application.



In the seventh part of the project, which is ongoing, we are continuing to investigate the ability of surfactant-based organized media to control the regiochemistry of Diels-Alder reactions.⁸ We are utilizing sulfone surfactant **18** as the precursor of surfactant diene **19**, in combination with dienophiles **20**.



With the quaternary ammonium head groups of both **19** and **20** at a surfactant aggregate-water interface, regioisomer **21** should be the preferred product, as opposed to **22**. Preliminary results indicate little or no regiochemical selectivity in the reactions of nonsurfactant analogues of **19** and **20**, whereas with **19** and **20a**, a 1.7:1 ratio of diastereomers **21** and **22** resulted, and with **20b**, a 2.7:1 ratio. At present we do not know which is the major isomer. But it appears the objective of the study is being at least partially realized.



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7. D. A. Jaeger and Y. M. Sayed, to be published.
8. D. A. Jaeger and J. Wang, to be published.

III. Publications

The publications under the contract correspond to references 1-6 above.

IV. Participating Scientific Personnel

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Postdoctoral Research Associates

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V. Inventions

None